

In the Claims:

Please cancel claims 14-16 and 21-27.

Please amend claims 3, 5-13, 17 and 20.

Please add new claims 28-31.

1. **(Original)** A method for preparing a protein-polymer conjugate comprising:
  - (a) contacting an insulin protein with a hydrophilic polymer in the presence of at least one organic solvent and at least one metal chelator, under conditions that promote the formation of a conjugate of the protein and the polymer; and
  - (b) isolating the conjugate.
2. **(Original)** The method of claim 1, wherein the insulin protein comprises human insulin.
3. **(Currently Amended)** The method of claim 1 or 2, wherein the hydrophilic polymer is selected from the group consisting of polyethylene glycol, polyethylene glycol/polypropylene glycol copolymers, polyoxyethylated glycerol, and linear, branched and amino-reactive derivatives thereof.
4. **(Original)** The method of claim 3, wherein the amino-reactive derivative is selected from the group consisting of an aldehyde, a N-hydroxy succinimide, a PNP-carbonate, and a benzotrizole terminated hydrophilic polymer.
5. **(Currently Amended)** The method of any of the preceding claims claim 1, wherein the hydrophilic polymer and insulin protein are contacted at a molar ratio of about 10:1-1:1.

6. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, wherein the organic solvent is selected from the group consisting of ethanol, methanol, DMSO, dioxane, DMF, and NMP.
7. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, wherein the organic solvent is present at a concentration of about 0.1 to 10%.
8. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, wherein the insulin protein and hydrophilic polymer are contacted at a protein concentration of about 0.1-5.0%.
9. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, wherein the insulin protein and hydrophilic polymer are contacted at a pH of about 5.0-7.5.
10. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, wherein the chelator is selected from the group consisting of polyvalent metal ion chelators, EDTA, deferoxamine (DEF), diethylenetriamine pentaacetic acid (DTPA), and bis(aminoethyl)glycolether N,N,N',N'-tetraacetic acid (EGTA).
11. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, wherein the chelator is present at a concentration of about 0.1-10 mM.

12. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, wherein the insulin protein and hydrophilic polymer are contacted at a temperature of about 4-50° C.

13. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, wherein the method further comprises the step of quenching formation of the conjugate prior to isolating the conjugate.

14-16. **(Cancelled)**

17. **(Currently Amended)** The method of ~~any of the preceding claims~~ claim 1, further comprising the step of encapsulating the conjugate in a biodegradable polymer.

18. **(Original)** A method for preparing an insulin-PEG conjugate comprising:

- (a) contacting insulin with PEG in the presence of at least one organic solvent and at least one metal chelator, under conditions that promote the formation of a conjugate of the insulin and PEG; and
- (b) isolating the conjugate.

19. **(Original)** The method of claim 18, wherein the insulin comprises human insulin.

20. **(Currently Amended)** The method of claim 18 or 19, wherein the PEG comprises an amino-reactive PEG derivative selected from the group consisting of an aldehyde, a N-hydroxy succinimide, a PNP-carbonate, and a benzotrizole terminated hydrophilic polymer.

**21-27. (Cancelled)**

28. **(New)** An insulin-PEG conjugate comprising PEG linked to insulin at the PheB1 amino terminus via a secondary amine.

29. **(New)** A poly(lactide-co-glycolide) (PLGA) microsphere encapsulating the insulin-PEG conjugate of claim 28.

30. **(New)** An insulin-PEG conjugate produced according to the method of claim 18.

31. **(New)** A F5000 insulin-PEG conjugate comprising PEG linked to insulin at the PheB1 amino terminus via a secondary amine.